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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A23L 2/52, 2/68, 1/304</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 98/32344</b> <b>(43) International Publication Date:</b> 30 July 1998 (30.07.98)
<b>(21) International Application Number:</b> PCT/US98/01432 <b>(22) International Filing Date:</b> 26 January 1998 (26.01.98) <b>(30) Priority Data:</b> 08/789,412 27 January 1997 (27.01.97) US <b>(71) Applicant:</b> ABBOTT LABORATORIES [US/US]; CHAD 0377/AP6D-2, 100 Abbott Park Road, Abbott Park, IL 60064-3500 (US). <b>(72) Inventors:</b> DeWILLE, Normanella, T.; 2580 Clairmont Court, Columbus, OH 43220 (US). CHANDLER, Michael, A.; 5359 Harvestwood Lane, Gahanna, OH 43230 (US). MAZER, Terrence, B.; 6897 Roundelay Road North, Reynoldsburg, OH 43068 (US). RAGAN, Robert, J.; 5679 Bull Run Court, Gahanna, OH 43230 (US). SNOWDEN, Gregory, Allan; 5600 Kean Road, Westerville, OH 43082 (US). GERAGHTY, Maureen, Elizabeth; 6090 Rocky Rill Road, Columbus, OH 43235 (US). JOHNSON, Catherine, Dubinin; 6080 Turkey Legs Court, Dublin, OH 43017 (US). <b>(74) Agents:</b> DIXON, J., Michael; Ross Products Division, Abbott Laboratories, Dept. 108140/DS-1, 625 Cleveland Avenue, Columbus, OH 43215-1724 (US) et al.		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> CALCIUM FORTIFIED LOW pH BEVERAGE		
<b>(57) Abstract</b>  Liquid beverages for supplementation of dietary calcium are disclosed. The beverages of this invention use calcium glycerophosphate as the source of calcium, acidulants, vitamin C.		

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**CALCIUM FORTIFIED LOW pH BEVERAGE****Technical Field**

The present invention relates to a clear liquid nutritional product which has a low pH and is  
5 fortified with calcium and vitamin C to meet 50%, most preferably, 100%, of the adult RDI for vitamin C  
in a 12-ounce (355 ml) serving and from 30-50% of the adult RDI for calcium in a 12-ounce serving.  
Most preferably, the beverage of this invention contains 30-50% of the RDI for calcium and 100% of  
the RDI for vitamin C in 355 ml.

**10 Background of the Invention**

Calcium is an essential nutrient; it is a major component of mineralized tissues and is required  
for normal growth and development of the skeleton and teeth. Over the last decade, calcium has  
enjoyed increased attention due to its potential role in the prevention of osteoporosis. Osteoporosis  
affects more than 25 million people in the United States and is the major underlying cause of bone  
15 fractures in post menopausal women and the elderly. "Optimal Calcium Intake," JOURNAL OF THE  
AMERICAN MEDICAL ASSOCIATION, 272(24): 1942-1948 (1994).

As used herein "osteoporosis" refers to a reduction in the amount of bone mass. Two  
important factors influencing the occurrence of osteoporosis are optimal peak bone mass attained in  
the first two to three decades of life and the rate at which bone mass is lost in later years. Adequate  
20 calcium intake is critical to achieving optimal peak bone mass and modifies the rate of bone mass loss  
associated with aging. Wardlaw, "Putting Osteoporosis in Perspective," JOURNAL OF THE  
AMERICAN DIETETIC ASSOCIATION, 93(9): 1000-1006 (1993).

Calcium requirements vary throughout an individual's lifetime with greater needs occurring  
during the period of rapid growth in childhood and adolescence, pregnancy and lactation, and in later  
25 adult life. Table 1 presents the optimal calcium requirements or Recommended Daily Intake (RDI)

which were established at a National Institute of Health (NIH) Conference on Optimal Calcium Intake, held June 6-8, 1994. "Optimal Calcium Intake," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 272(24): 1942-1948, at 1943 (1994). The participants at the NIH Conference considered former Recommended Dietary Allowances (RDA) (10th edition, 1989) for calcium intake as reference levels and used them as guidelines to determine optimal calcium intake in light of new data on calcium-related disorders.

**TABLE 1**  
**Optimal Calcium Intakes**

GROUP	OPTIMAL DAILY INTAKE (in mg of calcium)
<b>Infants</b>	
Birth-6 months	400
6 months-1 year	600
<b>Children</b>	
1-5 years	800
6-10 years	800-1,200
<b>Adolescents/Young Adults</b>	
11-24 years	1,200-1,500
<b>Men</b>	
25-65 years	1,000
Over 65 years	1,500
<b>Women</b>	
25-50 years	1,000
Over 50 years (post menopausal)	
On estrogens	1,000
Not on estrogens	1,500
Over 65	1,500
Pregnant and nursing	1,200-1,500

National consumption data indicate most females over the age of eleven, as well as elderly men, consume amounts of calcium below recommended levels. "Nationwide Food Consumption Survey, Continuing Survey of Food Intakes of Individuals," USDA NFCS, CFS II Report No. 86-93 (1988). According to the Second National Health and Nutrition Examination Survey, the median daily calcium intake for women in the United States was 574 mg. DIETARY INTAKE SOURCE DATA: UNITED STATES, 1976-80, Data From the National Health Survey, Series II, No. 231, DHHS Publication No. (PHS), pages 83-1681 (1983).

The preferred approach to attaining optimal calcium intake is through dietary sources. Dairy products are the major contributors of dietary calcium because of their high calcium content (e.g., approximately 250-300 mg/8 oz of cow's milk) and frequency of consumption. However, many persons, especially women, prefer to limit their intake of dairy products for several reasons: (a) they dislike the taste of milk/milk products; and/or (b) they have a lactose intolerance; and/or (c) they perceive that some dairy products are too high in fat or protein and may lead to weight gain. A number of calcium-fortified food products are currently available, including fortified juices, fruit drinks, breads and cereals.

To maximize calcium absorption, food selection decisions should include consideration of information on the bioavailability of the calcium contained in the food. Bioavailability (absorption) of calcium from food depends on the food's total calcium content and the presence of components which enhance or inhibit calcium absorption. Bioavailability of minerals in food has been traditionally tested by the balance method, which estimates absorption from the difference between ingested intake and fecal output. This approach works well for many nutrients where the difference between intake and excretion is large, but is less well suited for an element such as calcium. A decline in absorption from 30% to 20% could have profound nutritional significance but would be difficult to detect using the balance method. In contrast, isotopic methods estimate absorption directly from the appearance of the

ingested tracer in body fluids. Future clinical evaluations of the bioavailability of calcium from the liquid nutritional product of the present invention will use a state-of-the-art isotope tracer method.

Not all calcium salts are created equally. Calcium salts range from 9% elemental calcium in calcium gluconate to 40% calcium in calcium carbonate. Bioavailability depends on solubility. A new calcium delivery system, Calcium Citrate Malate (CCM) claims to be approximately six-times the solubility of either calcium citrate or calcium malate, both of which are themselves substantially more soluble than calcium carbonate. Smith, et al., "Calcium Absorption from a New Calcium Delivery System (CCM)," CALCIFIED TISSUE INTERNATIONAL, 41:351-352 (1987) relates an experiment in humans wherein calcium from CCM was absorbed significantly better than from either calcium carbonate or milk, 38.3% vs. 29.6% and 29.4% respectively. WO 91/19692 discloses a process for making a metastable calcium citrate malate.

The United States Food and Drug Administration (FDA) has advised that, in order for calcium-containing food ingredients in conventional foods or calcium supplement products to be considered eligible to bear the authorized calcium/osteoporosis health claim, they must meet the requirements in §101.14, which include that they have been shown to the FDA's satisfaction to be safe and lawful under the applicable safety provisions of the Act (56 FR at 60699). Of the 36 or more calcium-containing ingredients identified by the agency as currently in use, the FDA advised that only the following 10 compounds had been demonstrated to be safe and lawful for use in a dietary supplement or as a nutrient supplement: calcium carbonate, calcium citrate, calcium glycerophosphate, calcium oxide, calcium pantothenate, calcium phosphate, calcium pyrophosphate, calcium chloride, calcium lactate, and calcium sulfate (56 FR at 60691).

For some individuals, calcium supplements may be the preferred way to obtain optimal calcium intake. Although calcium supplements are available in many salts, calcium carbonate is usually recommended because it contains more elemental calcium per gram than any of the other salts. The disintegration and dissolution characteristics of commercial calcium carbonate preparations, which vary

widely, may produce important differences in calcium absorption. Other problems with using large amounts of calcium carbonate is that it can lead to constipation and abdominal distention. When problems arise, calcium lactate or calcium citrate are advised. A popular commercially available calcium supplement is TUMS 500™ which is distributed by SmithKline Beecham, Pittsburgh, Pennsylvania, U.S.A. and is labeled as providing 500 mg of elemental calcium (from calcium carbonate) per tablet.

U.S. 4,786,510 and U.S. 4,992,282 disclose the use of calcium citrate malate in a beverage or dietary supplement fortified with iron.

WO 92/19251 and WO 92/21355 disclose the use of calcium citrate malate in a low pH beverage, and suggests that vitamin D be added to such a beverage along with oil flavors or weighing oil.

EP 0 486 425 A2 discloses a liquid oral nutritional formulation which contains carbohydrates, protein, fat, fiber, calcium, and vitamin D, and has a pH of about 3.5 to 3.9. However, this publication teaches that high amounts of micronutrients such as calcium or magnesium may impair the palatability of the product, and should contain the recommended daily allowance of these nutrients in about one liter of product. A commercially available product in accordance with this patent publication is distributed by Sandoz Nutrition under the trade name CITRISOURCE® and is labeled as providing 570 mg of calcium and 210 IU of vitamin D per liter. By way of comparison, one embodiment of a beverage according to the present invention contains at least 1,408 mg of calcium per liter or 0.14 wt. %.

U.S. 4,737,375 teaches beverage concentrates and beverages having a pH of 2.5 to 6.5, preferably 3.0 to 4.5, which contains calcium derived from calcium citrate malate. The acidulants used in this prior art beverage are chosen from mixtures of citric acid, malic acid and phosphoric acid, and the weight ratio of total acids to calcium is in the range of 4 to 7.

Two commercially available beverages which are labeled as being protected by U.S.

4,737,375 are: (1) Sunny Delight® With Calcium which is distributed by Procter & Gamble, Cincinnati,

Ohio 45202 U.S.A.; and (2) HAWAIIAN PUNCH®, DOUBLE C which is distributed by Sundor Brands, Inc., Cincinnati, Ohio 45202 U.S.A.. According to the "Nutrition Facts" on the labels of these commercially available products: (a) neither product contains vitamin D; (b) neither product contains any fat; (c) a 240 mL (8 fluid ounce) serving of Sunny Delight® With Calcium provides 30% of the recommended daily intake (RDI) of calcium; (d) a 240 mL (8 fluid ounce) serving of HAWAIIAN PUNCH®, DOUBLE C provides 15% of the recommended daily intake of calcium; and (e) and a 240 mL (8 fluid ounce) serving of each of these products provides 100% of the recommended daily intake of vitamin C. Per the product labels, these percent daily values are based on a 2,000 calorie diet. Samples of each of these products were tested regarding their pH values: the pH value of the HAWAIIAN PUNCH® DOUBLE C was 3.91; and the pH value of the Sunny Delight® With Calcium was 4.05.

GB 2 196 253 A discloses a beverage containing calcium and vitamin D. A water soluble non-toxic calcium salt is used in a quantity sufficient to provide in the final beverage a calcium ion content of from  $1.0 \times 10^{-2}$  to  $40 \times 10^{-2}\%$  w/w (0.01-0.4 wt. %).

U.S. Patent 5,597,595, claims liquid beverage concentrates that contain calcium glycerophosphate as the calcium source and a vitamin D emulsion. While the '595 patent is a valuable contribution to the art, products made via its teachings suffer from disadvantages. Products containing both calcium glycerophosphate and the vitamin D emulsion are cloudy. A cloudy drink is unacceptable to most consumers. They think that the product has spoiled or has been contaminated in some manner and will not consume it. Products made according to the instant invention do not suffer from this advantage.

The '595 patent does not indicate the source of the cloudiness. In column 24, at lines 20-55, it indicates that solutions of calcium glycerophosphate formed crystals when allowed to stand. Further, at column 26, lines 36-45, it indicates that vitamin D is not soluble aqueous solutions and that emulsifiers must be used to maintain it in solution.



The present inventors have discovered a solution to the problems associated with the drinks of the '595 patent. Clear calcium beverages can be manufactured by both removing the vitamin D and its associated emulsifiers, as well maintaining the pH of the beverage below 4.6. Such beverages are clear over a normal shelf life for food products. These beverages have excellent bioavailability of calcium and no stability problems on extended storage have been noted.

GB Patent 1,118,606 discloses a dosage unit for oral administration for the treatment of hemorrhoids comprising calcium glycerophosphate, vitamin D, vitamin C, vitamin B and piperazine phosphate.

U.S. Patent 5,500,232 to Keating discloses calcium fortified acid beverages. This patent teaches a calcium source that is a combination of calcium hydroxide and calcium glycerophosphate and the acidulant is a combination of citric acid and fumaric acid. Keating further teaches that in order to have acceptable storage stability it is necessary that the product contain as its calcium source a combination of calcium hydroxide and calcium glycerophosphate. Further the product must contain both citric acid and fumaric acid as acidulants. The present inventors have discovered quite unexpectedly that products having perfectly acceptable stability can be manufactured utilizing calcium glycerophosphate as the sole calcium source. Further, the inventors have unexpectedly discovered that fumaric acid is not required in such a product to achieve acceptable shelf life. Such products have superior taste and are thus more likely to be consumed on a regular basis.

## Summary of the Invention

In general this invention relates to clear liquid, ready to consume low pH beverages that provide at least 30%, more preferably 50% of the RDI for calcium and at least 50%, most preferably 100% of the RDI for vitamin C in one serving (12-oz or 355 ml.) One aspect of this invention resides in the discovery that high levels of calcium can be supplied through the use of calcium glycerophosphate in a low pH (2.8 to 4.6) beverage without product stability problems and unpleasant flavors.

Thus, there is disclosed a clear liquid beverage comprising water, calcium glycerophosphate, vitamin C and an acidulant, the beverage has a pH of from about 2.8 to 4.6 and wherein the beverage contains from about 7.2 to 18% by wt. calcium on a dry weight basis.

The acidulants used to lower the pH of the beverage can be those commonly used in the food and beverage industry to impart tart and/or sour tastes. A combination of citric and lactic acids are preferred. More preferred is a 75% by weight lactic acid -- 25% acetic acid acidulant. The beverage of this invention may also contain ascorbic acid, preservatives such as potassium benzoate, flavoring agents and sweeteners. The preferred sweetener is aspartame as it demonstrates a synergistic effect with CaGP in providing a pleasant taste and mouth feel to the inventive beverage. Other natural and artificial sweeteners can be used, for example acesulfame K.

In a preferred embodiment of the invention the beverage consists essentially of water; 10-18% by wt. calcium on a dry weight basis, said calcium is derived from calcium glycerophosphate; vitamin C; an acidulant mixture comprising 75% by wt. citric acid and 25% by wt. lactic acid; a preservatives; sweeteners and flavoring agents; said beverage has a pH of about 3.1 to about 4.0 and provides at least 50% of the RDI for calcium and vitamin C for an adult in about 355 ml.

If the RDI for calcium is 1000 mg/day for post menopausal women over 50 years of age and the inventive beverage supplied 100% of the calcium RDI in one service, then the beverage will contain 5.91 g of CaGP per 355 ml (12-oz.). The same beverage may also provide 100% of the RDI for vitamin C (RDI = 60 mg/day) in one serving, thus it would contain 60 mgs of ascorbic acid per 355 ml. In similar fashion, if the beverage according to this invention were designed to provide 30% of the RDI for calcium and vitamin C in one serving, it would contain 1.777g of CaGP and 18 mg of ascorbic acid per 355 ml. A beverage supplying 50% of the RDI for calcium and vitamin C in one serving would contain 2.96g of CaGP and 30 mg of ascorbic acid per 355 ml of beverage. In an additional embodiment of the invention, the beverage contains at least 120 IU of vitamin D per 355 ml of beverage.

The products of this invention solve a number of problems of the prior art calcium containing products. Unlike the products of United States Patent No. 5,597,595, these products remain clear. Unlike the products of the United States Patent No. 5,500,232, these products can utilize calcium glycerophosphate as the sole source of calcium.

5

#### Selection Of Ingredients Used In Practicing The Invention

The present invention provides high levels of calcium in a carbonated or a non-carbonated beverage. As used herein and in the claims the terms "liquid nutritional product" and "beverage" are understood to be synonymous. Further, it should be understood that any reference to a "beverage" or  
10 a "liquid nutritional product" of this invention refers to a clear product. "Clear" refers to an absence of cloudiness, transparency or the ability to readily see through the liquid.

As used herein and in the claims a "low pH beverage" is understood to refer to a beverage having a pH of less than 4.6. Beverages were manufactured by blending the beverage components with water. Some beverages were then carbonated and filled into standard 12-ounce soda aluminum  
15 cans. (Soda aluminum cans are coated in accordance with accepted industry standards to substantially reduce migration of aluminum into the contents of the can.)

Calcium Source. As used herein and in the claims the term "calcium" used alone refers to elemental calcium, the term "calcium salt" refers to a chemical composition containing elemental calcium, and "calcium source" refers to calcium and/or a calcium salt. The calcium salt used in the  
20 present invention is Calcium Glycerophosphate (CaGP) which is generally recognized as safe (GRAS) by the United States Food and Drug Administration (FDA) (21 CFR 170.3).

Calcium glycerophosphate (CaGP) can be described as a white, odorless, almost tasteless powder. Its solubility in water increases in the presence of citric and lactic acids, as stated in the Merck Index. The CaGP used herein was FCC III grade and was produced by Dr. Paul Lohman GmbH,

Emmerthal, Germany and distributed by Gallard Schlesinger Industries, Inc., Carle Place, New York, 11514, USA.

Another reason for selecting CaGP is its excellent calcium bioavailability. Churella, et al., "Relative Calcium (Ca) Bioavailability Of Ca Salts Used In Infant Formulas," THE FASEB JOURNAL, 4(3):A788 (1990) reports a study which determined the calcium bioavailability of four calcium salts. Rats were fed various diets containing different calcium salts for three weeks. At the end of the study, the right femur was removed and tested for calcium. As compared to a control, the relative calcium bioavailability was as follows: tricalcium phosphate 110%, calcium citrate 110% and CaGP 106%. Furthermore, studies reported by Hanning, et al, "Efficacy of Calcium Glycerophosphate vs.

Conventional Mineral Salts for Total Parenteral Nutrition in Low-Birth-Weight Infants: A Randomized Clinical Trial," AMERICAN JOURNAL OF CLINICAL NUTRITION, 54:903-908 (1991), and Draper, et. al., "Calcium Glycerophosphate as a Source of Calcium and Phosphorous in Total Parenteral Nutrition Solutions," JOURNAL OF PARENTERAL AND ENTERAL NUTRITION, 15(2):176-180 (1991) showed in low birth weight infants and piglets, respectively, that CaGP is as effective as calcium gluconate as a source of calcium in total parenteral nutrition (TPN) solutions and could be used to prevent under mineralized bones in low birth weight infants.

Yet another reason for selecting CaGP was its high solubility which facilitates a larger calcium intake per serving. A number of calcium salts were evaluated for their functionality in the liquid nutritional product of the present invention: dicalcium phosphate, monocalcium phosphate, calcium chloride, tricalcium phosphate, calcium citrate, calcium carbonate, CaGP, and D-gluconic acid (hemicalcium salt). Aqueous solutions containing 500 mg of calcium per 240 mL (8 oz.) serving (2110 ppm) were prepared and the pH was adjusted to pH 3.5 and pH 5.0. Results indicated that solubility of calcium salts varied and only calcium carbonate, calcium chloride, CaGP, and D-Gluconic acid, remained soluble at pH 3.5 for at least one month. In this evaluation solubility was determined by a

visual examination. At pH 5.0 all samples formed crystals over time. The results of this solubility study are presented in Table 2.

**TABLE 2**  
**Solubility Of Calcium Sources**

5

<u>Salt</u>	<u>At Time of Manufacture</u>		<u>1 MONTH</u>	
	<u>pH 3.5</u>	<u>pH 5.0</u>	<u>pH 3.5</u>	<u>pH 5.0</u>
Dicalcium Phosphate	insoluble	insoluble	insoluble	insoluble
Monocalcium Phosphate	insoluble	insoluble	insoluble	insoluble
Calcium Chloride	soluble	soluble	soluble	insoluble
Tricalcium Phosphate	insoluble	insoluble	insoluble	insoluble
Calcium Citrate	insoluble	insoluble	insoluble	insoluble
Calcium Carbonate	soluble	partially soluble	soluble	insoluble
CaGP	soluble	soluble	soluble	insoluble
D-Gluconic-Acid*	soluble	soluble	soluble	partially Soluble

\* Hemicalcium salt

10 Experiments were repeated with calcium carbonate, CaGP, and calcium chloride in a complete liquid nutritional product matrix, i.e., in conjunction with aspartame, a flavor system and vitamin C. The pH range evaluated was 3.5-4.5. At the lower end of the pH range all calcium sources were soluble at time of manufacture. After one month it was observed that as the pH increased, calcium carbonate formed crystals. In addition, it appeared that the CaGP had a synergistic effect with aspartame  
15 regarding sweetness. Calcium chloride was completely soluble throughout the pH range but its bitter flavor made it unacceptable for the liquid nutritional product of the present invention. Calcium lactate

was evaluated in subsequent experiments. Although its solubility was excellent it provided astringent and mineral salt-type notes to the taste of the beverage that made it undesirable.

Still another reason for selecting CaGP is the fact that a beverage matrix containing this calcium salt requires the addition of less acid to achieve a pH below 4.0. Acidity is desired in the liquid nutritional product of the present invention for several reasons such as: to maintain the calcium salt solubility, to complement flavor, to control microbial growth, and to enhance the role of preservatives, specifically potassium benzoate or sodium benzoate. On the other hand, too much acidity can result in increased tartness and sourness that make the product undesirable from a sensory point of view.

When calcium salts are added to a liquid nutritional product, the solution resists changes in pH and more acid is needed to bring down the pH than in commercially available beverages with no calcium fortification.

Aqueous solutions of various calcium salts were prepared to deliver 500 mg of elemental calcium per 12-oz. (355 mL) serving (1408 ppm) and the pH adjusted to pH 3.5 with citric acid.

Titrateable acidity was determined by measuring the amount of 0.1N NaOH needed to raise the pH to 8.3 in a 40g sample containing 1,409 mg/Kg of a calcium source. The results presented in TABLE 3 indicate that, with the exception of calcium chloride, CaGP was the calcium salt that had the lowest titrateable acidity. Titrateable acidity is an indication of the total acidity of a beverage.

TABLE 3  
Titratable Acidity Of Calcium Sources

<u>Calcium Source</u>	<u>Titratable acidity mL of 0.1N NaOH</u>
Calcium Chloride	0.7
CaGP	43.5
Calcium Lactate	47.1
Tricalcium Phosphate	48.6
Calcium Citrate Malate	53.2
Calcium Citrate	57.5
Calcium Hydroxide	60.6
Calcium Carbonate	61.4

5 CaGP, when dissolved in water, dissociates readily to provide "free" calcium ions and protonated glycerophosphate species. Acid-base buffering by monoprotonated glycerophosphate is effective only within the pH range from 4.1 to 8.1, and thus, CaGP exhibits insignificant buffering capacity at pH=3.6. On the other hand, anions, such as malate, tartrate, propionate or succinate, do provide buffer capacity at pH=3.6, and accordingly require more base or acid than CaGP for final  
10 adjustment of pH.

Yet another reason for selecting CaGP is the low aluminum content in commercially available CaGP. It has been theorized that chronic use of calcium supplements which have significant aluminum contents may constitute unnecessary metal exposure. Whiting, "Safety of Some Calcium Supplements Questioned," NUTRITION REVIEWS, 52(3):95-97 (1994). The aluminum content of some calcium  
15 sources is presented in TABLE 4.

**TABLE 4**  
**Aluminum Content Of Calcium Sources**

<b>Calcium Source</b>	<b>Aluminum Content in parts per million (ppm)</b>
CaGP	4.55 <sup>1</sup>
Calcium Hydroxide	300-400 <sup>1</sup>
CaCO <sub>3</sub> (from fossil shell)	4,400 <sup>2</sup>
CaCO <sub>3</sub> (from Dolomite)	171-315 <sup>2</sup>

<sup>1</sup> Values determined by analysis of commercially available compounds.

<sup>2</sup> Values from Whiting article.

Acidulants. Acids are commonly used in food and beverages to impart specific tart or sour tastes and to function as preservatives. A combination of citric and lactic acids are used in the liquid nutritional product of the present invention. Citric acid is the most widely used acid in fruit beverages in part because it blends well with these flavors. It is commercially manufactured by fermentation or by synthesis; either may be used in the practice of the present invention. When using fermented lactic acid, a purified form that is free of sugar residues is recommended due to its cleaner taste and clearer appearance. Food grade lactic acid is available in aqueous and crystalline forms.

Sweetener. The sweetener used in the beverages described in the Examples below is aspartame, but other artificial or natural sweeteners can be used in the practice of the present invention. Artificial sweeteners that may be employed include aspartame, saccharin, acesulfame-K and the like. Natural sweeteners that may be employed include sucrose, fructose, high fructose corn syrup, glucose, sugar alcohols, dextrose, maltodextrins, maltose, lactose, and the like but other carbohydrates can be used if less sweetness is desired. Mixtures of natural sweeteners, or artificial sweeteners, or natural and artificial sweeteners can also be used.

The amount of the sweetener effective in a product according to any aspect of the present invention depends upon the particular sweetener used and the sweetness intensity desired. In determining the amount of sweetener, any sugar or other sweetener present in the flavor component or product matrix should also be taken into consideration.



Studies have shown that the efficiency of calcium absorption can be enhanced two-five fold by oral administration of glucose polymer both in patients with intestinal calcium malabsorption and in normal subjects. Kelley, et al., "Effect of Meal Composition on Calcium Absorption: Enhancing Effect of Carbohydrate Polymer" GASTROENTEROLOGY, 87:596-600 (1984).

5 In another study using the triple-lumen intestinal perfusion technique, glucose polymer increased net calcium absorption fourfold. Bei, et al., "Glucose Polymer Increases and Equal Calcium Magnesium, and Zinc Absorption in Humans," AMERICAN JOURNAL CLINICAL NUTRITION, 44:244-227 (1986).

10 It is understood that a person of skill in the art may make a product in accordance with the invention containing glucose polymers or glucose.

Ascorbic Acid. Ascorbic acid, also known as vitamin C, is a required element in the beverage of this invention. Vitamin C is a white crystalline compound that is highly soluble in water. The stability of vitamin C decreases with increases in temperature and pH. A considerable quantity of the vitamin C content of foods is lost during processing, storage and preparation. Humans with vitamin C deficiency  
15 have what is known as scurvy. They typically lose weight, are easily fatigued, have swollen joints and have fragile bones.

There has been great difficulty in establishing the human requirements for vitamin C. The recommended dietary allowances of the Food and Nutrition Board of the National Research Council  
are 30 mgs per day for 1-3 month old infants, 80 mgs per day for growing boys and girls, and 100 mgs  
20 per day for pregnant and lactating women. Many nutritionists believe that the human intake of ascorbic acid should be many times more than that intake level which produces deficiency symptoms.

Flavor. As used herein, the term "flavor" includes both natural and artificial flavors. The particular amount of the flavor component effective for imparting flavor characteristics to the beverage of the present invention can depend upon the flavor(s) selected, the flavor impression desired, and the

form of the flavor component. The amount of flavor employed in a product according to any aspect of the present invention is within the skill of one in the art and depends on the flavor intensity desired.

Preservatives. Most microbial spoilage of low pH beverages is caused by aciduric and acidophilic organisms like certain varieties of yeasts and molds. For this reason, preservatives with anti-microbial activity such as benzoic and sorbic acids are added to soft drinks. Usage levels of these acids or their salts range from 0.025 to 0.050 percent, depending on the nutritive substances present and the pH of the finished beverage. The antimicrobial activity of these preservatives has been shown to be largely pH dependent. They are least effective under neutral conditions but their activity increases considerably with decreasing pH. For example, by reducing the pH value from 4.5 to 3.0, the preservative effect of benzoic acid is increased by nearly three times.

Carbonation. The amount of carbon dioxide in a beverage according to the present invention depends upon the particular flavor system used and the amount of carbonation desired. Usually, carbonated beverages of the present invention contain from 1.0 to 4.5 volumes of carbon dioxide. Preferred carbonated beverages contain from 2 to 3.5 volumes of carbon dioxide. The beverages of the present invention can be prepared by standard beverage formulation techniques. To make a carbonated beverage carbon dioxide can be introduced either into the water mixed with the beverage syrup or into the drinkable diluted beverage to achieve carbonation. It should be understood, however, that carbonated beverage manufacturing techniques, when appropriately modified, are also applicable to non-carbonated beverages.

## EXAMPLE 1

### Organoleptic Testing

This experiment was conducted to evaluate the impact of various sources of calcium on the taste of the final beverage. Using a procedure similar to that set out in Example 3 below, beverages were prepared using calcium sources as set out in Table 5. Table 5 also sets out the amount of

calcium in each beverage, the level of aspartame, the pH of the resulting beverages and the titratable acidity of each beverage.

TABLE 5

Beverage No.	Mineral Source	Calcium mg/100 g	Aspartame mg/L	pH (2 runs)	Titrateable Acidity (ml of 0.1 N NaOH to reach pH 8.3) (avg. of 2 runs)
1	calcium lactate	110	529	3.68 3.81	29.2 29.0
2	calcium gluconate	99	528	3.87 3.87	25.7 25.0
3	calcium citrate malate	103	531	3.88 3.58	36.6 36.4
4	calcium glycerophosphate	105	532	3.85 3.67	34.3 34.6

5

The beverages of Table 5 provide about 33% of the RDI for calcium in a 12-oz. serving. Each beverage was evaluated for Fullness, Balance, Sweet, Sour and Aftertaste by a panel of individuals trained in sensory evaluation.

Balance is a measure of the degree of blend or the balance of the character notes in the beverage. Balance is affected by the intensities of the character notes as well as the order of appearance of the notes. It is rated on a scale of one (unblended) to seven (blended).

10

Fullness refers to the fullness and body of flavor or the degree of complexity. It is rated on a scale of one (thin) to seven (full).

Sweet is a measure of the level of sweet basic taste. The reference standard for sweet intensity, measured on a scale from one to seven, is sucrose solutions of 5% for slight (3), 10% for moderate (5), and 15% for strong (7).

15

Sour is a measure of the level of sour basic taste. The reference standard for sour intensity, measured on a scale from one to seven, is citric acid solutions of 0.05% for slight (3), 0.10% for moderate (5), and 0.20% for strong (7).

Aftertaste is a measure of all sensations remaining one minute after swallowing. This is measured on a scale of one (none) to seven (strong). This includes basic tastes, feeling factors, and aromatics. The panelists recorded the character notes in their comments.

Of all the profiles, Balance is the most important and is generally regarded as the most pertinent measure of a beverage's consumer acceptance. All beverages were evaluated chilled (about 10°C).

The results of this investigation are set forth in Table 6.

TABLE 6

Organoleptic Evaluations

(Values Reported Are Averages From The Panel)

Beverage No.	Fullness	Balance	Sweet	Sour	After Taste
1- calcium lactate	3.6	3.6	4.3	4.3	2.7
2- calcium gluconate	3.0	2.0	4.5	2.5	4.3
3- calcium citrate malate	3.3	3.6	4.0	4.3	3.0
4- CaGP	3.8	4.3	4.0	4.2	2.7

This investigation demonstrates that calcium glycerophosphate is the preferred source of calcium from a taste perspective. With reduced aftertaste and high levels of balance, the use of CaGP provides a highly acceptable liquid composition for supplying at least 30%, more preferably 50% and most preferably 100% of the RDI for calcium in a 12-oz. serving.

Beverage No. 2 (calcium gluconate) stood out among the samples as the most different. It had the lowest balance score, which was due to a high mineral salt and phenolic off-notes. Even though Beverage No. 2 was less sour than the other beverages, this did not improve the Balance or Fullness because the off-note was so noticeable.

**EXAMPLE 2**  
**Calcium Fortified Beverage Without Vitamin D**

One aspect of this invention resides in the use of CaGP and acidulants to produce a beverage  
5 that will supply at least 30%, more preferably 50% and most preferably 100% of the RDI for calcium in  
one twelve ounce serving. In one embodiment of this invention, the beverage contains no vitamin D as  
the use of this vitamin requires the presence of emulsifiers which complicate the manufacture of the  
beverage.

To produce a 1000 kg batch of ready-to-drink beverage, 987.31 kg of water was placed in a  
10 vessel fitted with an agitator. At ambient temperature, 0.30 kg of potassium benzoate was added and  
allowed to completely dissolve. The following ingredients were then added in the order listed. Each  
ingredient was completely dissolved before the next ingredient was added.

	Potassium Citrate	0.15	kg
	Citric Acid	2.89	kg
15	Lactic Acid	1.41	kg
	Aspartame	0.55	kg
	Calcium Glycerophosphate	6.06	kg
	Coloring Agents	0.0019	kg
	Natural and artificial flavors	1.00	kg
20	Ascorbic acid	0.33	kg

The ascorbic acid was added just before filling into 12-oz. aluminum cans.

25

**EXAMPLE 3**

~~—~~ An alternative method to the single vessel method set forth in Example 2 is the "addition of  
slurries" method. In the "addition of slurries" method, four slurries are prepared in separate vessels and  
then combined to form the final beverage. This approach is more practical than making one large  
batch, and is the preferred method of preparation.

30

Four slurries were made using the ingredients and amounts set forth in Example 2, except that  
the water was divided equally between the four vessels. Each ingredient was allowed to dissolve prior  
to the addition of the next ingredient.

5	Slurry #1	1)	potassium benzoate
		2)	potassium citrate
	Slurry #2	1)	citric acid
		2)	lactic acid
3)		aspartame	
4)		calcium glycerophosphate	
10	Slurry #3	1)	coloring agents
		2)	natural and artificial flavors
	Slurry #4	1)	ascorbic acid

Each slurry was pumped to a larger tank and the resulting blend was well mixed. Slurry #4,  
15 with the ascorbic acid, was added about 2 minutes before carbonation.

#### EXAMPLE 4

The beverages prepared in Example 2 and 3 were carbonated prior to filling into aluminum cans. The solutions were de-aerated and then transferred to a "carbo-cooler" where they were cooled and carbonated to approximately 2.5 volumes of carbon dioxide.

20

#### EXAMPLE 5 Beverage Concentrate Or Syrup

Using the ingredients and amounts set forth in Example 2, except that 16.7% by weight of water was used, a beverage syrup was prepared using the one vessel method. Each ingredient was  
25 completely dissolved prior to the addition of the next ingredient.

Using the procedure set forth in Example 3, a beverage syrup was made, except that 16% by weight of the recited amount of water was divided between the four vessels.

Preparation of the final beverage was accomplished through blending the syrup with water at a 1 to 5 ratio using a continuous metering device called a volumetric proportioner.

**EXAMPLE 6**  
**Beverage With 50% Of RDI For Calcium And Vitamin C**

5           In this experiment a low pH, non-caloric, carbonate beverage was prepared using Diet 7Up® concentrate mix as the base. The following ingredients were combined in the order listed. Each ingredient was completely dissolved before the next ingredient was added.

INGREDIENT	AMOUNT
Water	9.93 Kg
Diet 7Up® Concentrate	1.8 Kg
CaGP	129 g
Ascorbic Acid	1.48 g
Acid Solution	60 ml

10           The acid solution consisted of 24.4 g of 50% by wt. citric acid, 25.4 g of 75% phosphoric acid by wt. and 50.2 g of 85% lactic acid by wt. The mixture was placed in a carbonation cylinder and cooled to about 1-2°C. Carbon dioxide was then injected to approximately 3 volumes. 8 oz (240 ml) bottles were filled and capped. The beverage was clear and colorless. The CaGP was extremely soluble in  
15           this matrix and did not precipitate or cause any negative flavor notes. This beverage contained about 50% of the RDI for calcium and about 100% vitamin C in one serving (12 oz).

## We claim:

1. A clear liquid beverage consisting essentially of:

- a. water;
- b. calcium glycerophosphate;
- 5 c. vitamin C;
- d. sweeteners;
- e. flavoring agents; and
- f. an acidulant, said beverage having a pH in the range of about 2.8 to 4.6 and wherein said beverage contains from about 7.2 to 18.0% by wt. calcium on a dry weight basis
- 10 and wherein said beverage contains at least 50% of the RDI for calcium and vitamin C for an adult in about 355 ml.

2. A clear liquid beverage comprising:

- a. water;
- 15 b. calcium glycerophosphate as the sole source of calcium;
- c. vitamin C; and
- d. acidulants, wherein the said acidulants are a mixture comprising lactic acid and citric acid.

20 3. A beverage according to claims 2-10 wherein said calcium glycerophosphate is present at a concentration of about 1.77-5.91g/355ml.

4. A beverage according to any of claims 2 to 10 wherein said vitamin C is present at a concentration of about 18-60mg/355 ml.

25



5. A beverage according to any of claims 2 to 10 wherein the pH is in a range of from about 2.8-4.6.

5 6. A beverage according to any of claims 2 to 10 wherein the beverage further comprises a flavoring agent.

7. A beverage according to any of claims 2 to 10 wherein the beverage further contains aspartame.

10 8. A beverage according to any of claims 2 to 10 wherein the beverage is in the form of a concentrate.

9. A beverage according to any of claims 2 to 10 wherein the beverage is in a ready to consume form without additional dilution.

15

10. A liquid beverage according to any of claims 2-10 further comprising a glucose polymer.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/01432

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A23L2/52 A23L2/68 A23L1/304

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A23L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 31130 A (ABBOTT LABORATORIES) 10 October 1996 see page 13, line 1-3 see page 34, paragraph 2 see page 34, paragraph 3 - page 35, paragraph 1 see tables 18-21 see claims 1,2,6,7,9-13,15,17	1-10
A	US 5 500 232 A (K.R.KIM) 19 March 1996 see column 3, line 40-50 see column 4, line 14-16 see claims	1-10

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
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Date of the actual completion of the international search

23 April 1998

Date of mailing of the international search report

08/05/1998

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## INTERNATIONAL SEARCH REPORT

Internat. .... Application No

PCT/US 98/01432

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE WPI Section Ch, Week 8234 Derwent Publications Ltd., London, GB; Class D13, AN 82-71895E XP002063213 & SU 876 097 B (MAMCHUR F I) , 1 November 1981 see abstract ---	1-10
A	DATABASE WPI Section Ch, Week 8251 Derwent Publications Ltd., London, GB; Class D13, AN 82-11210J XP002063214 & SU 908 308 B (PRESERVE IND FOOD) , 28 February 1982 see abstract ---	1-10
A	DATABASE WPI Section Ch, Week 8618 Derwent Publications Ltd., London, GB; Class D13, AN 86-117187 XP002063215 & JP 61 058 560 A (NIPPON OILS & FATS CO LTD) , 25 March 1986 see abstract -----	1-10

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Information on patent family members

International Application No

PCT/US 98/01432

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